

**PERSONAL REFLECTIONS ON THE STARTUP OF THE WOMEN'S INTERAGENCY HIV STUDY (WIHS) NCAB**

By Marta Santiago

The Women's Interagency HIV Study (WIHS) was conceived from the concern in the rising number of HIV positive women and the lack of research. The National Institute of Health (NIH) would become the main funder for the WIHS and in 1993 six cities would make up the WIHS; they were Chicago, Bronx, Brooklyn, DC, Los Angeles, and San Francisco. The goal was to enroll 2,600 women, 2/3 HIV positive and 1/3 HIV negative.

By request of the funders, a National Community Advisory Board (NCAB) was formed and was composed of participants. The purpose of the new NCAB was to provide investigators and study leadership specific participant feedback. There was no better way to know how a study is going than to have the actual participants speaking directly with study investigators.

As WIHS was getting into gear for their first face-to-face meeting was held in New York on a wintery day in 1993; each site had a study participant that would serve as the representative for their respective site. The snow was plentiful on that day when the Executive Committee (EC) which included the Principal Investigators (PI's), Project Directors (PD's) of all six WIHS sites would come together. This is also when the first WIHS NCAB meeting took place in a separate conference room.

The new NCAB spent hours getting to know one another and of their sites, but the main goal was to develop bylaws for the new WIHS NCAB. The newly drafted bylaws were introduced to the Executive Committee before the end of the day. Eventually, these meetings would take place twice a year, Spring and Fall. It was determined at that time that the WIHS NCAB representative would be selected by each site, and the terms for WIHS NCAB chair, co-chair would rotate sites each year alphabetically by site.

The NCAB representatives' main responsibilities were to share information received from study scientific representatives to study participants, and vice versa from

study participants their concerns and feedback. The NCAB representative would attend study working group calls, gather any new information or questions, and share the knowledge learned with the study participants in workshops offered by the study site. Most of the sites developed newsletters that would also be shared with all other WIHS sites.

Eventually, sites were able to select alternate and a co-alternate rep to share some of the NCAB representatives' responsibilities, which included being on working group calls. One needed to make time for calls and meetings, and being part of the NCAB was not always easy. The representatives really needed to keep up with the scientific aspects of the study. Keeping up with medical and scientific terms was a challenge, but layman terms were requested by the NCAB for everything brought out from the study to the participant.

Being part of the WIHS NCAB has been an honor but not easy. Although some women have expressed interest in the NCAB, for many other priorities came first; taking care of family, young and or old, looking for a paying job, having a job, finding affordable child care, decent and affordable shelter, etc. These study participants were the back bone of their family.

**WHY IS SO MUCH BLOOD DRAWN?**

By Beth D Jamieson, PH.D.

There they are in front of you, those tubes with different colored tops just waiting for you to roll up your sleeve and donate blood. You must wonder "Why blood?" and "Why so much?"

Understanding what blood is may help explain why it's so important to study. Blood is made of both fluid and cells. The fluid (called plasma) helps to carry nutrients that our body needs to all the places that need it. Plasma also helps carry away the waste from our cells and organs so the body can get rid of it. By collecting plasma, doctors can measure some of the products of different organs. Looking at those products can tell a doctor whether those organs are healthy or not.

Blood is also made up of red and white cells. Red blood cells carry oxygen from the air we breathe to all the organs and cells of our body. The white blood cells include cells of the immune system, like T-cells. T-cells fight germs like HIV and the virus that causes COVID-19. HIV can kill some T-cells so scientists and doctors count T-cells to make sure HIV treatments are working. B-cells are also part of the immune system. B-cells make proteins called antibodies which fight germs. Antibodies move around the body in the plasma. Scientists and doctors measure antibodies to know if someone has been infected with a specific germ or made a good immune response to a vaccine. Scientists collect and study T and B-cells to learn more about how these cells work. This is information can help science in many ways like in vaccine development.

Clearly there are many important reasons to study blood. But we can't study the plasma and cells together. Each blood collection tube has a different chemical in it. Some of those chemicals help separate fluid from cells. One chemical will prepare the blood for one type of test, but a different chemical prepares the blood for different type of test. The color of the tube-top tells the clinic what type of test the blood will be used for. Also, some of the blood will be stored for future research so that scientists can continue to study the various ways that HIV may affect different conditions. That's why so many tubes of different colors are used. Hopefully, the next time you roll up your sleeve, you will understand how important it is for the MWCCS to study blood and why we collect so many different tubes.

### **INTRODUCTION TO THE STAR PROJECT: STUDY OF TREATMENT AND REPRODUCTIVE HEALTH IN WOMEN**

By Queen Hatfield

The Study of Treatment and Reproductive Health in Women (STAR) cohort seeks to answer questions related to the effects of HIV infection and HIV-related medical conditions on women of reproductive age. Today, STAR is expected to continue until the year 2024 and builds on

the work of the Women's Interagency HIV Study (WIHS). Recently, WIHS transitioned to combine with the Multicenter AIDS Cohort Study (MACS), which is a cohort of gay and bisexual men, to form the MACS/WIHS Combined Cohort Study (MWCCS). Utilizing the backbone of the MWCCS, STAR seeks to obtain information on reproductive age women living with HIV (WLWH) and those at risk for HIV infection. This study focuses on the Southern region and plans to recruit and retain 2,000 reproductive-age women who are HIV-positive and HIV-negative.

The STAR cohort protocol is being conducted in six Southern MWCCS sites/subsites: Miami, Washington, DC, Chapel Hill, Atlanta, Birmingham, and Alabama/Jackson. Participants come twice a year to complete interviews, brief physical exams, and specimen collection, with an expected visit time of two to four hours, outside of the normal MWCCS visit. If you are located in the southern region and want more information, please visit the MACS/WIHS Combined Cohort Study website, hover over the Community tab, and click Study Locations.

Queen is a participant in STAR and has attended her first visit. "My visit for STAR was not too bad. I was in the waiting room for less than 5 minutes until STAR staff placed me in a room with a computer. Study staff left the room and through WebEx, we were able to do my consent and to update my demographical information. Once complete, staff collected a urine sample from me. I entered the exam room, changed into a gorgeous hospital gown to complete my physical exam.

The physical exam consisted of a blood draw, height, weight and blood pressure. In comparison to my regular MWCCS visit, this physical exam is more of a do-it-yourself specimen collection. I collected several swabs from the throat, butt and vaginal area.

The STAR team is working out the final details for the repository which will hold certain specimens. So, staff

was unable to draw all of the blood needed for the study. I was told that I would be contacted to return to collect these specimens at some point. After all of the exam was done, I changed clothes and was off back to work. I was treated with care, along with some good conversation about life. Overall, it was a quick visit.”

#### **MWCCS INVESTIGATOR BIO - DR MICHAEL PLANKEY**

By Dan Fitzgerald

Dr. Michael Plankey has been instrumental in the creation and organization of the National Community Advisory Board (NCAB) for the Multicenter AIDS Cohort Study (MACS) and has an impressive research career with many scientific contributions.

Dr. Plankey received a PhD in Biometry with a focus on nutritional epidemiology from the Medical University of South Carolina. In 1995, he came to Washington, DC to do a post-doctoral fellowship at the CDC-National Center for Health Statistics to pursue this interest in obesity and body composition using data from the National Health and Nutrition Examination surveys.

After the fellowship and looking for a job, his research transitioned to infectious disease epidemiology working in the Viral Epidemiology Branch of the National Cancer Institute using data from the Multicenter Hemophilia Study, MACS, WIHS (Women’s Interagency HIV Study) and the DC-NYC Clinical Cohort Study. He worked with Dr. Jim Goedert and Bob Biggar using early HIV genetic data to understand disease progression in the setting of hepatitis B, C, E and G co-infection.

Since 2006 when he joined the faculty in the Department of Medicine, Division of Infectious Diseases as an investigator with both the former MACS (Baltimore-DC JHU) and WIHS (Washington, DC, Georgetown), Dr. Plankey’s research interest in HIV disease has been varied including but limited to studying the intersection of recreational drug use and risky sexual behaviors with poor health outcomes, hearing and vestibular function loss, heart failure and myocardial fibrosis, liver fibrosis and hepatosteatosis using Fibroscan, nicotine metabolism and pre-ART initiation among MACS

smokers, and energy expenditure and fatigue using special MRI techniques of lower extremities, and identifying psychosocial strengths and how they promote health and well-being among middle-aged and aging MACS men. He has over 218 scientific papers to his credit.

Dr. Plankey led the creation and organization of the National Community Advisory Board (NCAB) for the former Multicenter AIDS Cohort Study (MACS). Currently he is the co-investigator liaison with Dr. Deborah Weiss, PhD for the MACS WIHS Combined Cohort Study (MWCCS) NCAB. He provides a unique perspective to the NCAB both as an investigator and participant. The NCAB truly appreciates his contribution to its work.

Outside of his professional activities, Dr. Plankey is an avid movie and theater goer, enjoys travel photography, and is investigating his German-French-Irish genealogy.

The NCAB has been fortunate to have Michael supporting their efforts.

#### **WHY IS HIV SO HARD TO CURE IN A NUTSHELL?**

By Marc C.E. Wagner



HIV makes it to the core of the nut. This is symbolic to show it passes barriers to get into very sensitive areas in our body. Once inside, it makes changes that allows it be there even though drugs to treat it keep it from replication. We need to get to the seed in order to reach a cure.

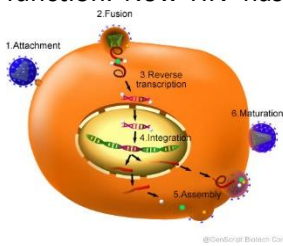
We need to understand the life cycle of HIV in order to appreciate the challenges in reaching a cure that is safe and scalable for everyone living with it. HIV infects primarily CD4 T helper cells but can also infect other cells acting as a source of continuing infection.

HIV is a retrovirus and what this means is that it begins its life as Ribonucleic Acid (RNA). Once HIV attaches and fusion takes place, this RNA with the help of an enzyme

called reverse transcriptase converts the RNA to deoxyribonucleic acid (DNA).

This DNA makes its way to the nucleus of the cell where another enzyme called integrase allows for the HIV DNA to become a permanent part of the cells own DNA.

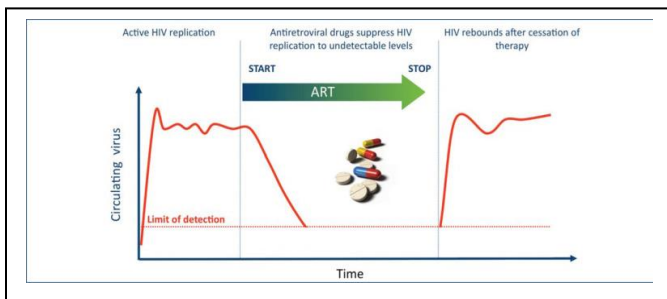
DNA is the blue-print for everything the cells need to function. Now HIV has inserted its own instruction for producing more virus into this same blue-print. Not all of the cells that get infected with HIV start producing virus. Infected cells not producing virus are not recognized as abnormal and escape being targeted by the immune system for removal. CD4 T helper cells can make more of themselves by duplicating the blue-print and dividing into two cells from one. This process is called mitosis. Everything to continue the life cycle of HIV gets copied as well making what is called the reservoir larger in numbers.



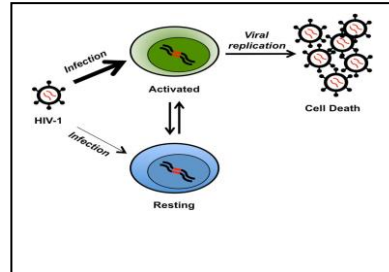
<https://www.frontiersin.org/articles/10.3389/fmicb.2018.03107/full>

The virus life cycle is completed when the blue-print is read back to RNA and more virus buds off and is released into the surroundings.

Medications used to treat HIV are highly effective on interfering with the production of more virus particles. If you stop taking these medications, there is a rapid increase in virus production. This tells us that taking these medications alone will not lead to a cure for HIV.



There are two directions that can happen when HIV infects its target cell. It can be infected and lead right into viral replication and death of that cell. It can also infect its target cell and go into a resting state. This is the challenge facing HIV cure research efforts.



Two individuals have been cured of HIV. However, the means by which this was accomplished is not scalable to all those infected with HIV. They were cured by

a bone marrow transplant from a donor who has a natural resistance to infection by HIV. One of the main co-receptors that HIV using to infect cells is controlled by the Delta 32 gene. Individuals lacking this gene do not make the CCR5 receptor thus not allowing HIV to infect their cells.

These two cases along with others called Elite Controllers because they seem to control the virus without the need of daily medications gives us all hope.

*The sources for the graphics in this article are:*

- <https://www.genscript.com/antibody-news/genScript-joins-the-hiv-vaccine-development.html>
- <https://www.nytimes.com/2020/06/03/nyregion/coronavirus-above-ground-pools.html>
- <https://www.sciencedirect.com/science/article/pii/S2055664020304908>
- <https://www.frontiersin.org/articles/10.3389/fmicb.2018.03107/full>

**THE NIH AND MWCCS RELATIONSHIP – PART 1**

*This is the first of three parts of a Q&A with Sean Altekruze and Gerald Sharp, two representatives of the NIH who are also members of the MWCCS Executive Committee.*

Was there a specific funding source for the MWCCS (e.g., NIAID)? The National Institutes of Health (NIH) Revitalization Act of 1993 instructs the Office of AIDS Research (OAR) to allocate appropriated AIDS research



funds to NIH Institutes based on how their research mission aligns with the [NIH Strategic Plan for HIV and HIV-Related Research](#). Currently NIH receives about \$3 billion a year in federal funds to support HIV research; half goes to the National Institute of Allergy and Infectious Diseases (NIAID), and the other half is split among the other NIH institutes.

The Plan provides a roadmap for NIH's HIV/AIDS research program, based on NIH scientific [research priorities](#). The Plan guides NIH investment, building on progress and opportunities to advance research to end the HIV/AIDS pandemic.

### Why is that institute is interested in funding the study?

The OAR is mandated to allocate funds for HIV/AIDS research. These funds are distributed by experts at OAR, with tremendous interest in assuring the best possible HIV research, to nearly all 27 NIH Institutes and Centers.

### Which institute funded it before, and why did it change?

The NIAID was the Primary Steward for the MACS and WIHS studies from their inception until April 2019, when stewardship for the CCS was transferred to the National Heart, Lung, and Blood Institute (NHLBI), and the MACS and WIHS studies were combined into a single study: the MACS/WIHS Combined Cohort Study (MWCCS). This change was made because many of the research questions that the cohort addresses have shifted as effective drug therapies have been developed and research interests have changed from studying the acute manifestations of HIV infection to studying the chronic HIV co-morbidities affecting mental health, and diseases of the liver, kidney, heart, lung, and blood as well as and sleep disorders. The MWCCS research agenda is broad, thanks to co-funding from 12 other institutes, besides NIAID and NHLBI, including the National Cancer Institute ([NCI](#)), National Institute on Aging ([NIA](#)), Eunice Kennedy Shriver National Institute of Child Health and Human Development ([NICHD](#)), National Institute of Dental and Craniofacial Research ([NIDCR](#)), National Institute on Drug Abuse ([NIDA](#)), National Institute of Mental Health ([NIMH](#)), National Institute of Neurological Disorders and

Stroke ([NINDS](#)), National Institute of Nursing Research ([NINR](#)) National Institute on Minority Health and Health Disparities ([NIMHD](#)), National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institute on Alcohol Abuse and Alcoholism (NIAAA), and the National Institute on Deafness and Other Communication Disorders (NIDCD).

Was there a chance that an institute would not fund the continuation of the study? Yes, it's possible that one of the co-funding NIH institutes could decide to spend their HIV dollars on some other HIV study. This is why the MWCCS investigators work hard to make sure that each co-funding institute's HIV research questions are addressed.

How does NIH get funding? And how does the funding flow down to sub orgs (e.g., NIAID)? Congress appropriates and the President signs legislation to fund each Federal Department, including Health and Human Services, and this legislation also mandates how these HHS funds will be distributed to agencies such as the NIH. The NIH HIV budget is distributed to Institutes in accordance with the [NIH Strategic Plan for HIV and HIV-Related Research](#).

What percentage of the overall NIH (or NIAID) is the MWCCS project? The current NIH budget is approximately \$40.3 billion per year. The costs of funding the MWCCS infrastructure and supporting ongoing studies at the 14 MWCCS sites is approximately \$50m/year. In addition to this, over a hundred investigators have successfully competed for NIH funds with additional study ideas. The total cost of these funded projects that involve MWCCS participants and their stored biologic specimens is another \$50m per year. The total cost of about \$100m annually to support the MWCCS cohort and the hundreds of research studies being conducted makes up about 0.25% of the total NIH budget.

How do they decide how to fund something? NIH's goal is always to rank research applications submitted for funding based on both their quality and their likely

clinical impact on people living with HIV. There are several approaches to determine the merit of competing research proposals. A standard method is to assemble a panel of HIV experts from US universities (what NIH calls “peer review”) to review grant applications submitted by principal investigators at the 14 funded MWCCS sites. This is how the core MWCCS grants were evaluated. The additional NIH grants that support linked studies were also reviewed by HIV experts outside NIH. NIH staff at the NIH institutes supporting MWCCS can also decide to provide extra funds to support HIV studies without going through the formal peer review process by outside experts. This is how some MWCCS components, such as echocardiograms, were funded. This was also done to support COVID-19 research in the current pandemic where NIH decided to provide funding as quickly as possible because of the health emergency.

How often does the MWCCS grant get reviewed and re-funded? The MACS and WIHS Combined Cohort Study is in Year-3 of a 7-year funding cycle. Other grants supporting MWCCS research may have a two to five-year time line.

Is the grant for specific number of years? Grants are funded for varying durations of time. Grants that involve clinical research, such as MWCCS, are often funded for 5-years. The NIH Office for Extramural Research granted an exception to MWCCS, allowing the current funding cycle to continue for 7-years to enable implementation of the new unified science agenda.

**Are there other similar research projects like MWCCS that the NIH had funded for so many years?** MWCCS is the most important and longest running HIV cohort study. There are also other HIV cohort studies that investigate special HIV topics such as substance use or brain pathology that have been funded for long periods of time. There are other non-HIV cohort studies, such as the Framingham Heart Study that have been funded for decades. For example, the original Nurses’ Health Study was established in 1976, and the studies continue today

in their third generation, with more than 280,000 participants enrolled.

### ABOUT THE MWCCS NCAB

By Dan Fitzgerald

MWCCS National Community Advisory Board (NCAB) which is a volunteer-led and staffed group of study participants to supporting the study and its outcomes. The NCAB bylaws state five key goals for the group:

- Identify pertinent issues of research not currently addressed by the MWCCS scientific agenda.
- Provide feedback to the MWCCS Executive Committee regarding strengths and weaknesses of study visit operations and procedures.
- Provide feedback on MWCCS’s research activities during the approval process.
- Communicate scientific results to MWCCS participants.
- Support local community advisory boards.

NCAB members are representatives of local Community Advisory Boards (CABs) that are nominated at the site-level to represent them at the national level. Generally, each site has a CAB that meets to address similar goals as the NCAB, but are focused at the individual site level activities. Some CABs are more active than others, but all are important to help make the study experience better for all of us participants. Some CABs also sponsor local site educational programs and social programs for the benefit of participants. If you are interested in learning more about your local CAB, or volunteering to serve on it, contact your local study staff, or ask about the CAB at your next study visit.

The NCAB meets monthly via zoom to address topics and issues pertinent to the study and its participants. The NCAB also has representatives that serve on the MWCCS Executive Committee and Steering Committee. These are two of the key leadership and oversight committees for the study. We also have two key NCAB standing

committees that address science & research topics and another to create content and support the newsletter and NCAB website.

One of the key activities of the Science & Research Committee is review of proposed research Concept Sheets. Concept Sheets are submitted by researchers seeking MWCCS support for their proposed research; this can include utilizing existing participant data already collected during site visits, collecting new data, or have new study tests be performed. After reviewing and discussing the research proposal, including research goals and the burden on the participant, the NCAB committee makes a recommendation to MWCCS with participant feedback, concerns or issues with the proposed research proposal.

This newsletter is an example of something the NCAB publishes. Member of the Newsletter Committee also meet via zoom to discuss what should be included in each issue. Most newsletter articles are written and edited by the committee members. We are dedicated to providing interesting and news-important articles that we think will be of interest to other study participants. We feel the newsletter is a great recruitment tool as most sites are looking to recruit new participants.

We look forward to any feedback you may have and hope to one day see you on a CAB, the NCAB, or one of our committees.

**BY THE NUMBERS: STUDY ENROLLMENT UPDATE**

By Amanda Long

MWCCS enrollment began in October 2020 and as of July 30, 2021 we have enrolled 3,008 participants:

- 2,828 continuing participants from the former MACS and WIHS studies and,
- 180 new enrollees.

Everyone who participated in the MACS study or WIHS study is eligible to re-enroll in the MWCCS.

Enrollment by Gender (as of July 30, 2021):

Gender	Continuing Participants	New Enrollees	Total
Cisgender Man	1,172	110	1,282
Cisgender Woman	1,652	66	1,718
Transgender Man	2	-	2
Transgender Woman	2	4	6
<b>Total Participants</b>	<b>2,828</b>	<b>180</b>	<b>3,008</b>

Our goal is to recruit 301 new enrollees by the end of this year and 1,590 total new enrollees by the 3<sup>rd</sup> quarter of 2023. We are recruiting new enrollees across the country with a focus on our southern sites (Atlanta, Birmingham/Jackson, Chapel Hill, and Miami). We recruit via other research studies, community organizations and support programs, local and state government programs, referrals from doctors, advertisements, and word-of-mouth. We could use your support in sharing your positive experiences in MWCCS and encouraging others to join.

**CALLING ALL CAB CHAIRS**

The NCAB will soon be reaching out to all the MWCCS CAB Chairs across the country to establish a regular communications channel to mutually share news and information. We have been working with site PDs and others to create a master list of the MWCCS CAB Chairs. In the interim, if you wish to confirm your site’s CAB Chair, send a quick note to [mwccsncab@gmail.com](mailto:mwccsncab@gmail.com).

**STUDY VISIT 102 PREVIEW**

By Amanda Long

Study visit 102 (V102) will be similar to V101 (which goes through September, 2022), with the addition of some

new tests and surveys. The Visit 102 wave will last for one year (from October 1, 2021 to September 30, 2022) with each participant completing two visits within that period: (1) a “core” visit consisting of interviews (including follow-up COVID surveys), the ACASI, exams, and specimen collection; and (2) a “short” visit consisting of an abbreviated interview, as well as pulmonary function testing and specimen collection for selected participants. Visit 102 will also include two mental health assessments (the CAT-MH at the core visit and the CIDI at a separate visit) and neuropsychological assessment at the core visit. Whether you have your core or short visit first in visit 102 will depend upon when you started visit 101.

In addition, some studies will be done at only selected sites on a smaller group of participants, such as the Hearing and Balance study, the Sleep Study, and the Vision Study. Please reach out to your local site staff and CAB representatives or [mwccs@jhu.edu](mailto:mwccs@jhu.edu) for more information about the study tests and questionnaires being done at your site during V102. More information about V102 tests and surveys is in the table below.

Test or Survey	V101	V102
<b>All sites</b>		
Core interviews	X	X
Physical exam & specimen collection	X	X
Covid Surveys	X	X
Fibroscan	X	X
Pulmonary Function (PFTs)		X
CIDI mental health assessment		X
Cat-MH mental health assessment		X
Neuropsychological Assessment		X
<b>Selected Sites</b>		
Hearing & Balance study		X

Test or Survey	V101	V102
Echo Reproducibility (heart test)		X
Brain MRI (brain images)		X
Sleep study		X
Vision study		X

**HOW TO REFER A FRIEND TO JOIN THE STUDY**

Many study sites are actively recruiting new participants as shown in the “By the Numbers” article in this issue. Each site has different recruitment goals and timelines but if you are aware of someone who might be a good candidate to become a participant in the study, please contact your local site study staff to find out how to make the referral. The study staff welcome the opportunity to speak with people who may be interested in participating and will be enrolling based on study eligibility criteria and site target requirements.

**HOW TO CONTACT THE NCAB**

If you have a question or wish to learn more how you may be able to volunteer to support the NCAB’s mission, send an email to the NCAB at:

**[mwccsncab@gmail.com](mailto:mwccsncab@gmail.com)**

For more information, you can also visit our website:

<https://statepi.jhspsi.jhsph.edu/mwccs/ncab/>

